

In the Claims

Claims 1-6 (Cancelled)

Claim 7 (Currently amended):

A method for sequencing a polynucleotide, comprising the steps of:

- (i) reacting a target polynucleotide with a helicase enzyme or a primase enzyme, under conditions suitable for enzyme activity; and
- (ii) detecting the interaction between the enzyme and a the nucleotide on the target polynucleotide, ~~by measuring radiation to thereby determine the sequence of the target polynucleotide, the detection being carried out by measuring a change in, or absorption of, radiation that occurs during the interaction.~~

Claim 8 (Previously added):

The method, according to claim 7, wherein the radiation is electromagnetic.

Claim 9 (Previously added):

The method, according to claim 7, wherein step (ii) comprises using surface plasmon resonance.

Claim 10 (Previously added):

The method according to claim 7, wherein step (ii) comprises using nuclear magnetic resonance.

Claim 11 (Previously added):

The method, according to claim 8, wherein step (ii) comprises using surface plasmon resonance.

Claim 12 (Previously added):

The method, according to claim 8, wherein step (ii) comprises using nuclear magnetic resonance.

Claim 13 (Previously added):

The method according to claim 7, wherein the enzyme is immobilised on a solid support.

Claim 14 (Currently amended):

A method for sequencing a polynucleotide, comprising the steps of:

- (i) reacting a target polynucleotide with a helicase enzyme and a primase enzyme under conditions suitable for enzyme activity; and
- (ii) detecting the interaction between the enzymes and a nucleotide on the target polynucleotide, ~~by measuring radiation to thereby determine the sequence of the target polynucleotide, the detection being carried out by measuring a change in, or absorption of, radiation that occurs during the interaction.~~

Claim 15 (Previously added):

The method, according to claim 14, wherein the radiation is electromagnetic.

Claim 16 (Previously added):

The method, according to claim 14, wherein step (ii) comprises using surface plasmon resonance.

Claim 17 (Previously added):

The method according to claim 14, wherein step (ii) comprises using nuclear magnetic resonance.

Claim 18 (Previously added):

The method, according to claim 15, wherein step (ii) comprises using surface plasmon resonance.

Claim 19 (Previously added):

The method, according to claim 15, wherein step (ii) comprises using nuclear magnetic resonance.

Claim 20 (Currently added):

The method according to claim 14, wherein the enzymes are immobilised on a solid support.

Claim 21 (Currently amended):

A sensor chip comprising an optically transparent material; a reflective film; and a helicase enzyme, a primase enzyme, or both a helicase enzyme and a primase enzyme, immobilised thereon, immobilized on said chip.

Claim 22 (New):

A method for sequencing a polynucleotide, comprising the steps of:

- (i) reacting a target polynucleotide with a helicase enzyme under conditions suitable for enzyme activity; and
- (ii) detecting the interaction between the helicase enzyme and the nucleotide on the target polynucleotide, to thereby determine the sequence of the target polynucleotide, the detection being carried out by measuring a change in, or absorption of, radiation that occurs during the interaction.

Remarks

Claims 7-21 were pending in the subject application. By this Amendment, claims 7, 14, 20, and 21 have been amended, and claim 22 has been added. The undersigned avers that no new matter is introduced by this Amendment. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 7-22 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

The applicant gratefully acknowledges the Examiner's indication that claims 7-21 will be examined together in the subject application.

Submitted herewith is a supplemental Information Disclosure Statement (IDS), including Form PTO/SB/08, and copies of the references cited therein. The applicant respectfully requests that the references cited in the supplemental IDS be considered and made of record in the subject application.

Claims 7-20 are rejected under 35 U.S.C. §112, second paragraph, as indefinite. The applicant respectfully submits that the claims are not indefinite. However, by this Amendment, the applicant has amended claims 7 and 14 to lend greater clarity to the claimed subject matter. Claims 7 and 14 now recite that the polynucleotide is sequenced by reacting the target polynucleotide with the enzyme(s) under conditions suitable for enzyme activity, and detecting the interaction between the enzyme(s) and the nucleotide on the target polynucleotide by measuring a change in, or absorption of, radiation that occurs during the interaction, thereby determining the sequence of the polynucleotide. Support for this amendment can be found, for example, at page 2, lines 21-25, of the subject specification as originally filed. The applicant respectfully submits that step (ii) of claims 7 and 14 sufficiently sets forth the accomplished goal of sequencing the polynucleotide. In view of the above remarks, and the amendments to the claims, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claim 7, 13, 14, and 20-21 are rejected under 35 U.S.C. §102(e) as being anticipated by Crute (U.S. Patent No. 5,958,696). The applicant respectfully submits that the Crute patent does not disclose or suggest the claimed invention.

As indicated above, claims 7 and 14 recite a method for sequencing a polynucleotide by reacting a target polynucleotide with a helicase enzyme and/or a primase enzyme under conditions suitable for enzyme activity, and detecting the interaction between the enzyme(s) and the nucleotide on the target polynucleotide by measuring a change in, or absorption of, radiation that occurs during the interaction, thereby determining the sequence of the polynucleotide. As indicated at column 3, lines 54-67, and column 4, the methods described in the Crute patent involve measuring the helicase inhibiting ability of a test compound, as opposed to sequence analysis of a target polynucleotide. The steps required for carrying out the methods of the subject invention, as recited in claims 7 and 14, are different from those of the Crute patent.

By this Amendment, claim 21 has been amended to recite that the sensor chip comprises an optically transparent material; a reflective film; and a helicase enzyme, a primase enzyme, or both a helicase enzyme and a primase enzyme, immobilized on the chip. Support for this amendment can be found, for example, at page 4, lines 22 and 23 of the specification as originally filed. The Crute patent describes solid support materials such as polystyrene, polyvinyl chloride, or polycarbonate, that are derivatized with a protein (see column 3, lines 37-56, and column 4, lines 11-33); however, the sensor chip of the claimed invention is not disclosed. It is well settled in patent law that, in order to anticipate under 35 U.S.C. §102, a single reference must disclose within the four corners of the document each and every element and limitation contained in the rejected claims. *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991). The applicant respectfully submits that the Crute patent does not teach or suggest every element of the applicant's claimed invention and, therefore, does not anticipate or render obvious the applicant's claimed invention. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Claims 8-12 and 15-19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Crute (U.S. Patent No. 5,958,696) in view of Densham (WO 99/05315). The applicant respectfully traverses this rejection, and submits that the subject invention is not obvious over the cited references.

There is no objective reason why the skilled person would combine the teachings of the Crute patent and the Densham publication to arrive at the subject invention. The Crute patent is concerned

with quantitative tests to measure the extent to which a compound inhibits helicase activity. The Densham publication is concerned with sequencing polynucleotides, but is specific for a polymerase enzyme. There is no objective reason why one of ordinary skill in the art would select the helicase disclosed in the Crute patent for use in the polynucleotide sequence analysis method disclosed in the Densham publication. In view of the fact that the Densham publication describes detecting the incorporation of a nucleotide onto a target strand, it is not obvious that a helicase, which functions by unwinding double-stranded DNA, would facilitate the objective of the claimed invention. The method of the subject invention has the advantage that it can be carried out without the need for the separate addition of individual nucleotide triphosphates. In addition, as stated at page 1, lines 21-24, of the specification, the problem of secondary structures that exist within polynucleotide molecules is reduced using the natural activity of a helicase enzyme.

As the Examiner is aware, it is well established in patent law that in order to support a *prima facie* case of obviousness, a person of ordinary skill in the art must find both the suggestion of the claimed invention, and a reasonable expectation of success in making that invention, in light of the teachings of the prior art. *In re Dow Chemical Co.*, 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988). In view of the remarks above, the applicant submits the art does not suggest the applicant's claimed invention and, even if there was a suggestion to use a helicase, the ordinarily skilled artisan would not have had a reasonable expectation of success in obtaining the applicant's claimed invention. Reconsideration and withdrawal of the rejection under 35 U.S.C. §103 is respectfully requested.

By this Amendment, the applicant has amended claim 20 to correct an obvious typographical error. The applicant has also added claim 22, which recites reacting a target polynucleotide with a helicase enzyme. Support for claim 22 can be found, for example, at pages 1-2 of the specification and the claims as originally filed.

In view of the foregoing remarks and amendments to the claims, the applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachments: Amendment Transmittal Letter
Supplemental Information Disclosure Statement, including Form PTO/SB/08, and
copies of references cited therein